Taking stock of herbicide-resistant crops ten years after introduction^{†‡}

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Abstract: Since transgenic, bromoxynil-resistant cotton and glufosinate-resistant canola were introduced in 1995, planting of transgenic herbicide-resistant crops has grown substantially, revolutionizing weed management where they have been available. Before 1995, several commercial herbicide-resistant crops were produced by biotechnology through selection for resistance in tissue culture. However, non-transgenic herbicide-resistant crops have had less commercial impact. Since the introduction of glyphosate-resistant soybean in 1996, and the subsequent introduction of other glyphosate-resistant crops, where available, they have taken a commanding share of the herbicide-resistant crop market, especially in soybean, cotton and canola. The high level of adoption of glyphosate-resistant crops by North American farmers has helped to significantly reduce the value of the remaining herbicide market. This has resulted in reduced investment in herbicide discovery, which may be problematic for addressing future weedmanagement problems. Introduction of herbicide-resistant crops that can be used with selective herbicides has apparently been hindered by the great success of glyphosate-resistant crops. Evolution of glyphosateresistant weeds and movement of naturally resistant weed species into glyphosate-resistant crop fields will require increases in the use of other herbicides, but the speed with which these processes compromise the use of glyphosate alone is uncertain. The future of herbicide-resistant crops will be influenced by many factors, including alternative technologies, public opinion and weed resistance. Considering the relatively few recent approvals for field testing new herbicide-resistant crops and recent decisions not to grow glyphosate-resistant sugarbeet and wheat, the introduction and adoption of herbicide-resistant crops during the next 10 years is not likely to be as dramatic as in the past 10 years. Published in 2005 for SCI by John Wiley & Sons, Ltd.

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1 INTRODUCTION

Ten years have passed since the first commercial introduction of transgenic herbicide-resistant crops in 1995. Herbicide-resistant crops generated by biotechnology were controversial before they were introduced, ^{1,2} although at that time others predicted potential economic and environmental benefits of this technology.^{3,4} Even though much has been written about all aspects of herbicide-resistant crops, only two previous collections of reviews have attempted to cover most of the topics associated with this technology.^{5,6} During the approximately 10 years since these books were published, much has happened regarding herbicide-resistant crops. This review is meant to provide a summary of the development, current status, and possible future of herbicideresistant crops as an introduction to the collection of papers on herbicide-resistant crops in this special issue of Pest Management Science.

2 A SHORT HISTORY

The use of synthetic herbicides in agriculture blossomed with the advent of selective, auxinic herbicides (eg 2,4-D) in the middle of the last century. Since then, pesticide manufacturers have striven to develop herbicides that would kill most or all of the problem weeds without injury to the crop for which the herbicide was intended. Over the last half of the 20th century, many classes of selective herbicides with a variety of modes of action were discovered, developed and marketed. Herbicide molecules were tailored to provide greater selectivity, efficacy and safety. In most cases, the commercialized product was a compromise between how much crop injury would be acceptable and the degree and species spectrum of herbicide activity against weeds. Some excellent nonselective herbicides were also developed (eg paraquat, glufosinate and glyphosate) that could be used when and/or where the crop was not growing or with less

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than perfect methods to prevent contact with the crop.

Prior to the advent of modern biotechnology, there was a limited effort to find or breed cultivars that were resistant to certain herbicides. An example of this approach is the soybean cultivar 'Tracy M' that is resistant to rates of metribuzin that cause unacceptable damage to other soybean varieties.⁷ There was never much interest in this approach, partly because, at that time, seed companies were not owned by herbicide manufacturers and had little incentive to breed for traits that were tied to another company's product.

Soon after the first weeds evolved resistance to herbicides, 8,9 scientists began to consider altering crops to make them resistant to herbicides. Initially, non-transgenic methods were used. For example, a breeding program was initiated to move resistance from a Brassica rapa L that evolved resistance to triazine herbicides to Brassica spp crops. 10 This approach was used to produce several triazineresistant canola varieties that were released in the 1980s, but no other triazine-resistant crops were developed. Triazine-resistant canola varieties are sometimes lower yielding and have poorer seedling vigor than susceptible varieties. The farmer had to weigh the value of inexpensive weed control with triazines against potential yield reductions. The advent of selective sulfonylurea herbicides for canola and the unwanted pleiotropic effects of the resistance mutation eventually greatly reduced the market share for triazine-resistant canola, except in Australia, where there is no good alternative to control wild radish (Raphanus raphanistrum L).

Since triazine-resistant canola was introduced, nontransgenic breeding methods such as whole-cell selection, mutagenesis and plant selection from natural populations have been used to produce sulfonylurearesistant soybeans, sethoxydim-resistant maize and several imidazolinone-resistant crops (Table 1).^{11–13} In each of these cases, the physiological basis of resistance has been a herbicide-insensitive target site. There have been no agronomically significant pleiotropic effects noted with the mutations upon which these products are based. All of these herbicides are already selective, so this technology has only added the crop to the list of naturally resistant plant species. In other words, weed management with these herbicide-resistant crops is very similar to that with selective herbicides to which crops are naturally resistant. Other selective herbicides must be used with those to which the crop has been engineered to be resistant. The most successful of these products has been imidazolinone-resistant crops, especially imidazolinone-resistant rice.¹⁴

In the early 1980s, the tools for producing transgenic crops were becoming available. Several companies saw the advantage of using this technology to produce crops resistant to very broad spectrum herbicides (eg glyphosate and glufosinate) or to herbicides for which mutation to a resistant form was problematic (eg

Table 1. Herbicide-resistant crops now available to farmers in North America

Herbicide	Crop	Year available
Bromoxynil	Cottonb	1995
	Canola ^b	2000
Cyclohexanediones (sethoxydim) ^a	Maize	1996
Glufosinate	Canola	1995
	Corn	1997
	Cotton	2004
Glyphosate	Soybean	1996
	Canola	1996
	Cotton	1997
	Maize	1998
lmidazolinones ^a	Maize	1993
	Canola	1997
	Wheat	2002
	Rice	2002
Sulfonylureas ^a	Soybean	1994
Triazinesa	Canola	1984

^a Not transgenic.

^b No longer available.

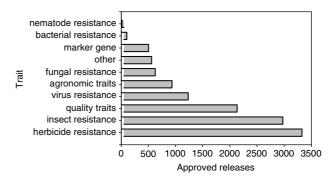


Figure 1. Total releases of transgenic crops for field testing approved by USDA-APHIS from 1987–late 2004.¹⁵ These data are only on permits that are acknowledged (notifications) or issued (full permit process). For practical purposes, there is no difference between full permits and notifications.

bromoxynil). Herbicide-resistant crops were the first major wave of transgenic crops. From 1988, 20–30% of the annual applications to the Animal and Plant Health Inspection Service of the US Department of Agriculture for permits to field test transgenic crops have been for herbicide-resistant crops, with a total of 26% of all permits from 1987 to 2004 (Fig 1). However, 36% of the approvals for deregulation (approval to commercialize) have been for herbicide-resistant crops.

One of the first transgenic HRCs available to farmers was bromoxynil-resistant cotton in 1995. 16 A transgene encoding a plasmid-encoded nitrilase from *Klebseilla ozaenae* was used to generate plants that rapidly degrade bromoxynil to non-toxic benzoic acid derivatives of bromoxynil. Subsequently, transgenic, bromoxynil-resistant canola was introduced in 2000. Neither of these herbicide-resistant crops captured much of the market share, but they have been very useful when the weed pressure from bromoxynil-susceptible weeds was a problem. Because bromoxynil

is not a broad-spectrum herbicide, introduction of these herbicide-resistant crops simply added another selective herbicide to those already available for use in these crops. This technology provided a means of extending the market share for an existing product, with relatively little additional regulatory costs for the herbicide itself. These herbicideresistant crops were recently removed from the market.

Introduction of transgenic crops made resistant to broad-spectrum, non-selective herbicides was rightfully perceived as a better strategy in terms of weed management and market share. The two herbicides that fitted this approach best were glyphosate and glufosinate. Both compounds are amino acid analogues that have molecular targets in amino acid biosynthesis pathways. In each case, there appears to be only one compound that is a viable herbicide targeting the molecular site. 17,18 Thus, the transgenic crop can be linked to the herbicide product of one company until the patent on the herbicide expires. If the company producing the herbicide and the herbicide-resistant crop are essentially the same, the seed and the herbicide can be sold as a package. There are many advantages of herbicide-resistant crops that are resistant to only one proprietary, non-selective herbicide over those that are each cross-resistant to several, similar selective herbicides owned by several companies.

An extensive effort was put into generating glyphosate-resistant crops, culminating in the use of the CP4 gene from Agrobacterium sp, which encodes a glyphosate-resistant form of 5-enolpyruvyl-shikimate-3-phosphate synthase (EPSPS).¹⁹ All commercial glyphosate-resistant crops except some maize varieties contain this gene. Glyphosate-resistant canola also contains a gene that encodes a glyphosate oxidoreductase (GOX) from the microbe Ochrobactrum anthropi (strain LBAA). This enzyme degrades glyphosate to glyoxylate, a ubiquitous and safe natural product, and aminomethylphosphonate (AMPA), a non-toxic compound. However, accumulation of AMPA in glyphosate-resistant soybeans has been correlated with mild phytotoxicity to the crop.²⁰ Why the GOX gene was used in canola but not other crops has not been made public. Some glyphosate-resistant maize varieties contain a mutated maize EPSPS transgene that imparts resistance.²¹

One of the first selectable transformation marker genes was the *bar* gene from *Streptomyces hygroscopicus*, the same organism that produces phosphinothricin, the natural form of glufosinate. This gene makes plants resistant to glufosinate by inactivating this herbicide through acylation. Many crop species have been successfully transformed with this gene. However, since 1997, only glufosinate-resistant canola, maize and cotton have been introduced in the USA (Table 1). Glufosinate-resistant canola has been grown in Canada since 1995.

3 CURRENT STATUS

3.1 Current products

To date, only five transgenes have been used in commercial crops to confer resistance to herbicides: CP4, GOX and the mutated maize EPSPS for glyphosate resistance, the gene encoding a nitrilase for bromoxynil resistance, and the *bar* gene for glufosinate resistance. Of the three herbicides (bromoxynil, glyphosate and glufosinate) used with herbicideresistant crops with these genes, only glyphosate has had a strong impact on weed management. With the discontinuation of bromoxynil-resistant crops by the company, only four transgenes and two herbicides are now being used with herbicide-resistant crops.

Glyphosate-resistant soybean has risen every year since its introduction in the USA, now at about 80% of the hectares treated (Fig 2). Glyphosate-resistant cotton has been similarly adopted. Approximately 75% of canola acreage in the USA was planted in glyphosate-resistant varieties in 2003.22 In these crops, glyphosate offers an economical and simple alternative that provides superior weed management. The adoption rate in maize $(ca\ 18\% \text{ in } 2004)^{23}$ has not been as dramatic because the economic advantages are not as clear. Despite great success with other glyphosate-resistant crops, glyphosate-resistant sugarbeet is not being grown by North American sugarbeet farmers, due to concerns about acceptance of sugar from transgenic plants by the confectionary industry. This herbicide-resistant crop was available for several years (Table 2), but not grown. Similar and other concerns have resulted in a decision by the company not to ask for deregulation of glyphosateresistant wheat in 2004.23

Glyphosate-resistant crops have led to a large increase in the use of glyphosate, an already popular herbicide. Patent rights for glyphosate expired in 2000, which was followed by a significant expansion in the commercialization of different salts and formulations of the herbicide. Competition caused by availability of generic glyphosate has led to a decline in glyphosate price, making the adoption of glyphosate-resistant

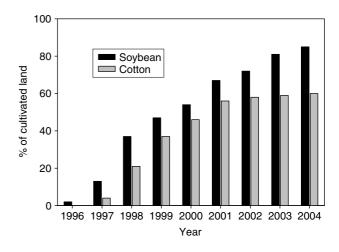


Figure 2. Adoption of glyphosate-resistant soybean and cotton in the USA by year.

Table 2. Regulatory approval for growing herbicide-resistant crops commercially world-wide as of 2003: only the first approval for a particular trait for a particular crop in a country is considered; this information was compiled from the agbios database, ²⁴ not all approvals have resulted in commercialization and sales

Crop	Herbicide	Country	Year approved ^a
Canola	Bromoxynil	Canada	1997
		Japan	1998
	Glufosinate	Canada	1995
		Japan	1996
		USA	1995
	Glyphosate	Australia	2003
		Canada	1995
		Japan	1996
		USA	1999
Cotton	Bromoxynil	Japan	1997
		USA	1994
	Glufosinate	USA	2003
	Glyphosate	Argentina	1999
		Australia	2000
		Japan	1997
		South Africa	2000
		USA	1995
	Sulfonylureas	USA	1996
Flax	Sulfonylureas	Canada	1996
		USA	1999
Maize	Glufosinate	Argentina	1998
		Canada	1996
		Japan	1997
		USA	1995
	Glyphosate	Argentina	1998
		Canada	1998
		Japan	1998
		South Africa	2002
		USA	1997
Rice	Glufosinate	USA	1999
Soybean	Glufosinate	Canada	1999
		Japan	1999
		USA	1996
	Glyphosate	Argentina	1996
		Brazil ^b	1998
		Canada	1995
		Japan	1996
		Mexico	1998
		South Africa	2001
		USA	1994
		Uruguay	1997
Sugarbeet	Glufosinate	Canada	2001
		USA	1998
	Glyphosate	USA	1998

^a First approval of any gene or transgenic event conferring resistance.

crops even more economical. Manufacturers of other herbicides for cotton and soybean have countered with reductions in prices for their products, ²⁵ possibly further accelerating the horizontal integration of the pesticide industry. Loss of some older products may be linked to the reduced value of the herbicide market. Smaller profit margins and the difficulty of capturing market share in soybeans have led to a significant decline in efforts to discover and commercialize new

herbicides. Finding new niches for existing herbicides, especially partnering those products with glyphosate programs, has a higher priority than discovery of new herbicides. Clearly, glyphosate-resistant crops have had a strong impact on weed management and the herbicide industry.

Bromoxynil- and glufosinate-resistant crops have had less influence than glyphosate-resistant crops. This is probably because the economic advantages have not been as dramatic as with glyphosate-resistant crops. In cotton, bromoxynil-resistant varieties never reached 10% of market share, except in certain geographic locations with weed problems that were particularly amenable to management with bromoxynil. The same company has propriety rights to both bromoxynil resistance and glufosinate resistance technology. Bromoxynil-resistant crops were recently withdrawn from the marketplace.

The above discussion summarizes the current situation in North America. Table 2 provides a summary of the current world-wide regulatory approval situation for herbicide-resistant crops. Approval has not always resulted in commercialization, as was the case with herbicide-resistant sugarbeet. In some cases there has been a long lag between approval and adoption. Adoption of glyphosate-resistant soybean has been close to 100% in Argentina and is increasing rapidly in Brazil, where it was only recently approved. Some glyphosate-resistant soybeans are grown in Uruguay and Mexico, and a small amount in South Africa. Although there have been some approvals for growing herbicide-resistant crops in some European countries, the adoption rates are almost zero, except in Romania, where glyphosate-resistant soybeans are grown. In summary, ten years after introduction of herbicideresistant crops, adoption of the technology has only been strong in three crops: soybean, cotton and canola. Furthermore, glyphosate-resistant crops have dominated the market for herbicide-resistant crops. Adoption has been strong in North America and two countries in South America.

3.2 Potential new herbicide-resistant crops

Genes exist to make crops resistant to most herbicide classes. 26-29 Furthermore, a new gene has been engineered by gene shuffling to make crops resistant to glyphosate.30 Many of these genes are patented, and considerable effort has been put into developing herbicide-resistant crops with certain of these transgenes. However, there is currently little effort to commercialize herbicide-resistant crops that are resistant to herbicides other than glufosinate and glyphosate. The number of regulatory approvals (deregulations) for new (new crop or new herbicide) commercialized herbicide-resistant crops declined after 1999 to a trickle (Fig 3). However, this trend is not much different from that for all other traits combined in the USA.15 No new crops have been added to the list of commercialized herbicide-resistant species since 1999. No approvals for deregulations

^b Reversed by courts, but reinstated in 2003.

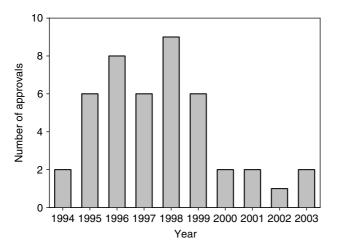


Figure 3. World-wide regulatory approvals for growing transgenic herbicide-resistant crops commercially. Only the first approval for a particular trait for a particular crop in a country is considered. Compiled from data in Table 2.

of a herbicide-resistant crop with a gene conferring resistance to a new herbicide have been granted world-wide since 1995 (Table 2). The petitioning of EPA for permits to field test herbicide-resistant crops continues to be 20–30% of permit applications for transgenic plants. The reasons for the reticence of the biotechnology industry to develop and market a new herbicide-resistant crop are provided by an article by Devine in this issue.³¹ Fundamentally, his view is that the high cost, lengthy development time and high risk due to many factors have been the primary reasons for the slow development and introduction of new herbicide-resistant crops.

3.3 Environmental effects

One of the chief criticisms of herbicide-resistant crops by early opponents was that they would lead to greater use of and reliance on herbicides. Studies can be found to support the view that herbicide use rates are greater with herbicide-resistant crops.³² However, there appear to be more studies that either support the opposite projection³³ or no dramatic changes in herbicide use.³⁴ Taken together, these studies suggest that the use rate (unit weight per unit area) of herbicides in herbicide-resistant crops is not substantially different from that in conventional crops. Bromoxynil, glyphosate and glufosinate are not low use-rate herbicides, but, when each is used with herbicide-resistant crops, they generally substitute for a suite of other herbicides. Often, some of the other herbicides are used as pre-plant or pre-emergence prophylactic treatments without knowing the potential weed pressure. All three of the herbicide-resistant crops herbicides are foliar-applied, post-emergence herbicides that can be used when and where they are actually needed. The reduction in costs of glyphosate and movement of more naturally resistant weed species into glyphosate-resistant crops may eventually lead to higher use rates of this herbicide.

There are several health and environmental benefits of the main two herbicides used in resistant crops, glyphosate and glufosinate. Both compounds are generally considered more toxicologically benign than many of the herbicides they replace. 35,36 Furthermore, both of these compounds have relatively short soil halflives, and neither moves easily to ground or surface water.³⁷ The most significant direct environmental effect has been from drift of sprayed glyphosate to non-target plants,³⁸ a problem with all foliar-applied herbicides. In the UK, farm-scale evaluations of herbicide-resistant crops have found that the more complete weed control with crops made resistant to non-selective herbicides sometimes does not leave sufficient weeds for natural fauna, thus reducing biodiversity.^{39,40} The mixed results of such studies have provided arguments for those both for and against herbicide-resistant crops.

Perhaps the most important environmental benefit of these compounds is that they have played a critical role in the movement to reduced-, minimum- and notillage agriculture. Loss of top soil due to tillage causes environmental damage that can last for centuries or even longer. In soybeans and cotton, tillage and incorporation of soil-applied herbicides have been important components of weed management. However, these practices are less useful with foliar-applied compounds that kill almost all weeds, such as glyphosate and glufosinate. Glyphosate-resistant soybeans have been instrumental in the rapid conversion to minimum tillage agriculture in the USA, and glyphosate-resistant cotton has contributed to the beginnings of minimum-tillage cotton. 41

Some have expressed concern about the potential effects of herbicide-resistant crops on soil health. There is no evidence that currently released herbicide-resistant crops are causing significant direct effects on stimulating or suppressing soil nutrient transformations in field environments.⁴²

The creation or spread of herbicide-resistant weeds as a result of herbicide-resistant crop use has been a concern of some environmentalists and farmers. Herbicide-resistant crops can influence herbicideresistant weeds in four ways. First, naturally herbicideresistant weed species can replace those species effectively controlled by the herbicide used with the resistant crop (sometimes called a weed shift). This is no different from what has happened with the advent of new herbicide classes. The only environmental impact of this would be the effect of an increase in use-rate of the herbicide-resistant crop herbicide or the addition of another herbicide that controls new species that have become a problem. Second, the herbicide used with the resistant crop can exert strong selection pressure on weed species, causing evolution of resistance. This has occurred once with glyphosate in glyphosate-resistant soybean, 43 although other glyphosate-resistant weeds have evolved in non-herbicide-resistant crops. The third possibility is that the herbicide-resistant crop becomes a weed in a different crop in which the herbicide to which the herbicide-resistant crop is resistant is used. For example, glyphosate is often used as a pre-plant treatment to eliminate winter weeds. A glyphosate-resistant volunteer from the previous growing season would not be controlled, but would be given an advantage by controlling the other vegetation. The first three types of weed problems with herbicideresistant crops are not new to farmers and pose no more environmental problems than those occurring since herbicides were introduced. However, there is a fourth possibility, that the herbicide resistance transgene could introgress into weedy relatives. This is a relatively new problem, as the natural resistance of crops to selective herbicides has rarely, if at all, introgressed into weedy relatives, partly because weedy relatives are usually also naturally resistant.

Movement of transgenes from herbicide-resistant crops into natural populations has been a legitimate concern of environmentalists. This is the only irrevocable effect that transgenic crops might have. A transgene that confers resistance to a herbicide is not likely to influence the behavior of a plant population in a natural environment where the herbicide is not used. Even if crossing of transgenic crops and wild relatives occurs at a very low frequency and the hybrids are very unfit, the herbicide will favor the survival of the few hybrids by eliminating competition. Similarly, the herbicide will protect the progeny of backcrossing until the gene has successfully introgressed into the wild species. Transgenes for herbicide resistance are almost certain to move from herbicide-resistant canola to weedy relatives.44 Transgene flow from cultivated rice to its weedy and wild relatives is also very likely.⁴⁵ Most crops have wild relatives with which they can interbreed somewhere on earth.

The most important environmental damage that a herbicide-resistant crop might cause would be to provide the selection agent (the herbicides) to speed the introgression of other transgenes that could provide an advantage in a natural habitat. Insect resistance and pathogen resistance are examples of transgenes that could alter ecological balances. Maize and cotton with transgenes encoding both insect and herbicide resistance have been approved for commercialization in the USA; however, introgression is not a concern for maize and cotton in the USA, as these crops will not interbreed with any USA wild species. In geographic locations where there is the potential for transmission of genes to wild relatives, there might be a concern with these herbicide-resistant crops. A more immediate problem is gene flow from herbicideresistant crops to non-transgenic crops of the same species. This has already caused problems in North America in crops that were meant to be kept transgenefree. Thus, there is a great need for fail-safe technology to prevent introgression from transgenic crops.

Some authors have raised concerns about horizontal transmission of transgenes (ie from the herbicideresistant crop to completely unrelated species). This phenomenon does occur in prokaryotes.⁴⁶ However,

there is little or no evidence that this process occurs between plant species.⁴⁷

3.4 Perceptions

As before herbicide-resistant crops were introduced, ^{1,2} transgenic crops (called genetically modified crops or GMOs by many) and particularly herbicide-resistant crops continue to be the focus of opposition by various special interest groups and a portion of the public, particularly in Europe. 48,49 The reasons for opposition are multiple and complex. Nevertheless, the adoption of herbicide-resistant crops world-wide has continued to expand. Even though very few herbicide-resistant crops are grown in Europe, significant amounts of herbicide-resistant crops are imported into Europe for animal feed. The widespread use of herbicide-resistant crops in the Western Hemisphere without significant mishap could eventually positively influence the public perception of them in parts of the world where the population is more negatively disposed toward this technology.

4 THE FUTURE

4.1 Future herbicide-resistant crops

As mentioned above, there are many patents for many types of transgenes to generate new types of herbicide-resistant crop. The regulatory approvals for herbicide-resistant crops by year suggests that there has not been a recent flurry of activity to gain approval of new ones, like there was in the late 1990s (Fig 3). The APHIS website has petitions to deregulate glyphosate-resistant bentgrass and alfalfa, two plant species not meant for direct human consumption. Petitions to field test other glyphosate-resistant turf grasses, as well as onion, are recent. There are recent petitions for field testing glufosinate-resistant turf grasses, sweet potato and wheat. Permits to field test crops resistant to hydroxyphenylpyruvate dioxygenase and protoporphyrinogen oxidase inhibitors have recently been approved. However, few petitions for field tests of herbicide-resistant crops have been translated into APHIS deregulation requests for their commercialization. The current status of these field testing requests can be accessed at: http://www.isb.vt.edu/CFDOCS/fieldtests2.cfm Clearly, there will not be a large number of new herbicideresistant crops in the near future.

4.2 Alternatives to herbicide-resistant crops

Will other technologies, either existing or in development, supplant herbicide-resistant crops? The old technologies are herbicides and tillage. New herbicides are being developed, albeit at a slower pace than in the past. Without the crop selectivity and broadspectrum capabilities of glyphosate and glufosinate, these new herbicides are not likely to significantly influence herbicide-resistant crop use. The efficiency of both herbicide use and tillage is being improved with precision agriculture, reducing both the amount

of herbicide used and the environmental damage done by tillage. The potential of this technology is great, and it could reduce the adoption of herbicide-resistant crops, should its cost be reduced and its efficiency improved.

Conventional approaches to biocontrol of weeds has had little impact on weed management. ⁵⁰ Research is under way to improve biocontrol agents with transgenes, ^{50,51} but this technology has considerably more environmental risk than herbicide-resistant crops. Research is also underway to make crops more allelopathic with transgene technology, with the hope that herbicide use would be substantially reduced with such varieties. ^{51,52} There is concern that introgression of transgenes for this type of trait into wild species could increase fitness in their natural ecosystems, with unpredictable consequences. Even if made successful and safe, this technology will not be available for at least 10 years.

4.3 Predictions

Clearly, there will not be a plethora of new herbicideresistant crops introduced over the next 5 years. There will probably be an increase in the adoption of some of the existing ones world-wide. Significant increases in weed resistance (natural, evolved, and introgressed) to the herbicides used with herbicide-resistant crops could slow further adoption of existing herbicideresistant crops, but could spur the introduction of new ones. Herbicide-resistant turf grasses could become a dominant product in the turf market, should they be deregulated, as such a product would make it relatively easy to maintain a turf monoculture, the ambition of almost all turf managers and home owners with lawns. Whether the recent concern about gene flow from glyphosate-resistant creeping bentgrass⁵³ will affect commercialization of this product remains to be seen.

A marked change in public attitudes about herbicide-resistant crops in the near future is not likely, but their neutral and/or favorable environmental aspects seem to be causing a shift toward governmental approval of transgenic crops, including herbicide-resistant crops, in some geographic areas. Adoption of herbicide-resistant crops in underdeveloped countries where hand weeding is prevalent and where parasitic weeds sometimes cause massive crop losses could have profound effects. In summary, I expect to see growth in herbicide-resistant crop use in the near future, but not the rapid growth that we have seen during the first 10 years of their availability.

Beyond the next 5 years, things are more uncertain. Improved precision agriculture and other transgenic approaches to weed management could dramatically change the weed management tools available. If so, public acceptance, safety and economics will be the driving factors in determining how these technologies compete with or complement herbicideresistant crops. Ten years ago no-one could have accurately predicted the progress and lack of progress

of herbicide-resistant crops over the ensuing 10 years. The next decade is likely to be just as unpredictable.

REFERENCES

- 1 Goldberg R, Rissler J, Shand H and Hassebrook C, Biotechnology's bitter harvest, Environmental Defense Fund, Biotechnology Working Group, New York (1990).
- 2 Krimsky S and Wrubel R, Agricultural biotechnology: an environmental outlook, Tufts University, Medford, MA (1993).
- 3 Duke SO, Holt JS, Hess FD and Christy AL, *Herbicide-resistant crops*, Comments from CAST, No 1991–1, Council for Agricultural Science and Technology, Ames, IA (1991).
- 4 Dyer WE, Hess FD, Holt JS and Duke SO, Potential benefits and risks of herbicide-resistant crops produced by biotechnology. *Hortic Rev* 15:367–408 (1993).
- 5 Duke SO (ed), Herbicide-resistant crops: agricultural, environmental, economic, regulation, and technical aspects, CRC Press, Boca Raton, FL (1996).
- 6 McClean GD and Evans G (eds), Herbicide-resistant crops and pastures in Australian farming systems, Bureau of Resource Sciences, Parkes, ACT, Australia (1995).
- 7 Barrentine WL, Hartwig EE, Edwards CJ and Kilen TC, Tolerance of three soybean (*Glycine max*) cultivars to metribuzin. *Weed Sci* **30**:344–348 (1982).
- 8 Ryan GF, Resistance of common groundsel to simazine and atrazine. Weed Sci 18:614-616 (1970).
- 9 Heap IM, The occurrence of herbicide-resistant weeds worldwide. Pestic Sci 51:235–243 (1997).
- 10 Hall JC, Donnelly-Vanderloo MJ and Hume DJ, Triazineresistant crops: the agronomic impact and physiological consequences of chloroplast mutation, in *Herbicide-resistant* crops: agricultural, environmental, economic, regulator, and technical aspects, ed by Duke SO, CRC Press, Boca Raton, FL, pp 107–126 (1996).
- 11 Dotray PA, Marshall LC, Parker WB, Wyse DL, Somers DA and Gengengach BG, Herbicide tolerance and weed control in sethoxydim-tolerant corn (*Zea mays*). *Weed Sci* 41:213–217 (1993).
- 12 Shaner DL, Bascomb NF and Smith W, Imidazolinone-resistant crops: selection, characterization, and management, in *Herbicide-resistant crops: agricultural, environmental, economic, regulator, and technical aspects*, ed by Duke SO, CRC Press, Boca Raton, FL, pp 143–157 (1996).
- 13 Saari LL and Mauvais CJ, Sulfonylurea herbicide-resistant crops, in Herbicide-resistant crops: agricultural, environmental, economic, regulator, and technical aspects, ed by Duke SO, CRC Press, Boca Raton, FL, pp 127–142 (1996).
- 14 Tan S, Evans RR, Dahmer ML, Singh BK and Shaner DL, Imidazolinone-tolerant crops: history, current status and future. Pest Manag Sci 61:246–257 (2005).
- 15 Animal and Plant Heath Inspection Service of the US Dept. Agriculture website: http://www.aphis.usda.gov/brs/brs_charts.html, accessed August, (2004).
- 16 Stalker DM, Kiser JA, Baldwin G, Coulombe B and Houck CM, Cotton weed control using the BXN system, in Herbicideresistant crops: agricultural, environmental, economic, regulator, and technical aspects, ed by Duke SO, CRC Press, Boca Raton, FL, pp 93–105 (1996).
- 17 Franz JE, Mao MK and Sikorski JA, Glyphosate: a unique global herbicide, ACS Monograph No 189, American Chemical Society, Washington, DC (1997).
- 18 Lydon J and Duke SO, Inhibitors of glutamine biosynthesis, in *Plant amino acids: biochemistry and biotechnology*, ed by Singh BK, Marcel Dekker, New York, pp 445–464 (1999).
- 19 Padgette SR, Re DB, Barry GF, Eichholtz DE, Delannay X, Fuchs RL, Kishore GM and Fraley RT, New weed control opportunities: development of soybeans with a Roundup Ready[™] gene, in Herbicide-resistant crops: agricultural, environmental, economic, regulator, and technical aspects, ed by Duke SO, CRC Press, Boca Raton, FL, pp 53-84 (1996).

- 20 Reddy KN, Duke SO and Rimando AM, Aminomethylphosphonic acid, a metabolite of glyphosate, causes injury in glyphosate-treated, glyphosate-resistant soybean. J Agric Food Chem 52:5139–5143 (2004).
- 21 Sidhu RS, Hammond BG, Fuchs RL, Mutz JH, Holden LR, George B and Olson T, Glyphosate-tolerant corn: the composition and feeding value of grain from glyphosate-resistant corn is equivalent to that of conventional corn (*Zea mays* L). J Agric Food Chem 48:2305–2312 (2000).
- 22 Gianessi L, Economic and herbicide use impacts of glyphosateresistant crops. *Pest Manag Sci* **61**:241–245 (2005).
- 23 Dill G, Glyphosate-resistant crops: history, status and future. Pest Manag Sci 61:219-224 (2005).
- 24 Web site: www.agbios.com/dbase.php?action=Synopsis, accessed August 12, (2004).
- 25 Nelson DC and Bullock GC, Simulating a relative environmental effect of glyphosate-resistant soybeans. *Ecol Econom* 45:189–202 (2003).
- 26 Gressel J, Molecular biology of weed control, Taylor & Francis, London (2002).
- 27 Arias RS, Netherland MD, Atul P and Dayan FD, Molecular evolution of herbicide resistance to phytoene desaturase inhibitors in *Hydrilla verticillata* and its potential use to generate herbicide-resistant crops. *Pest Manag Sci* 61:258–268 (2005).
- 28 Li X and Nicholl D, Development of PPO inhibitor-resistant cultures and crops. *Pest Manag Sci* **61**:277–285 (2005).
- 29 Matringe M, Sailland A, Pelissier B, Roland A and Zind O, p-Hydroxyphenylpyruvate dioxygenase inhibitor-resistant plants. Pest Manag Sci 61:269–276 (2005).
- 30 Castle LA, Siehl DL, Gorton R, Patten PA, Chen YH, Bertain S, Cho H-J, Duck N, Wong J, Liu D and Lassner MW, Discovery and directed evolution of a glyphosate tolerance gene. *Science (Washington)* 304:1151–1154 (2004).
- 31 Devine MD, Why are there not more herbicide-tolerant crops? *Pest Manag Sci* **61**:312–317 (2005).
- 32 Benbrook CM, Troubled times amid commercial success for Roundup Ready soybeans, *AgBioTech InfoNet*, Technical Paper No 4, Northwest Science Environmental Policy Center, Sandpoint, Idaho (2001).
- 33 Kleter GA and Kuiper HA, Environmental fate and impact considerations related to the use of transgenic crops, in *Chemistry of crop protection: progress and prospects in science and regulation*, ed by Voss G and Ramos G, Wiley-VCH Verlag GmbH & Co, Weinheim, pp 304–321 (2003).
- 34 Heimlich RE, Fernandez-Cornjo J and McBride W, Geneticallyengineered crops: has adoption reduced pesticide use? *Agricultural Outlook*, USDA Econ Res Serv AGO-273, August 13–17 (2000).
- 35 Williams GM, Kroes R and Munro IC, Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. *Regul Toxicol Pharmacol* **31**:117–165 (2000).
- 36 Ebert E, Leist KH and Mayer D, Summary of safety evaluation toxicity studies of glufosinate ammonium. Food Chem Toxicol 28:339-349 (1990).
- 37 Duke SO, Baerson SR and Rimando AM, Herbicides: Glyphosate, in *Encyclopedia of agrochemicals*, ed by Plimmer JR, Gammon DW and Ragsdale NN, John Wiley & Sons, New York (2003) http://www.mrw.interscience.wiley.com/eoa/articles/agr119/frame.html

- 38 Ellis JM, Griffin JL, Linscombe SD and Webster EP, Rice (*Oryza sativa*) and corn (*Zea mays*) response to simulated drift of glyphosate and glufosinate. *Weed Technol* 17:452–460 (2003).
- 39 Perry JN, Firbank LG, Champion GT, Clark SJ, Heard MS, May MJ, Hawes C, Squire GR, Rothery P, Woiwod IP and Pidgeon, JD, Ban on triazine herbicides likely to reduce but not negate relative benefits of GMHT maize cropping. *Nature* (*London*) 428:313–316 (2004).
- 40 Dewar AM, May MJ, Woiwod, IP, Haylock LA, Champion GT, Garner BH, Sands RJN, Qi A and Pidgeon JD, A novel approach to the use of genetically modified herbicide tolerant crops for environmental benefit. *Proc Royal Soc London, Ser B: Biol Sci* 270:335–340 (2003).
- 41 Carpenter J and Gianessi L, Herbicide tolerant soybeans: why growers are adopting Roundup Ready varieties. *AgBioForum* 2:65–72 (1999) available at http://www.agbioforum.org.
- 42 Motavalli PP, Kremer RJ, Fang M and Means NE, Impact of genetically modified crops and their management on soil microbially mediated plant nutrient transformations. *† Environ Qual* 33:816–824 (2004).
- 43 Feng PCC, Tran M, Chiu T, Sammons RD, Heck GR and CaJacob CA, Investigations into glyphosate-resistant horse-weed (*Conyza canadensis*): retention, uptake, translocation, and metabolism. *Weed Sci* 52:498–505 (2004).
- 44 Légère A, Risks and consequences of gene flow from herbicideresistant crops: canola (*Brassica napus* L) as a case study. *Pest Manag Sci* 61:292–300 (2005).
- 45 Chen LJ, Lee DS, Song ZP, Suh HS and Lu BR, Gene flow from cultivated rice (*Oryza sativa*) to its weedy and wild relatives. *Ann Bot* 93:67–73 (2004).
- 46 Jain R, Rivera MC and Lake JA, Horizontal gene transfer among genomes: the complexity hypothesis. *Proc Natl Acad Sci USA* 96:3801–3806 (1999).
- 47 Kim YT, Park BK, Hwang EI, Yim NH, Kim NR, Kang TH, Lee SH and Kim SU, Investigation of possible gene transfer to soil microorganisms for environmental risk assessment of genetically modified organisms. J Microbiol Biotechnol 14:498-502 (2004).
- 48 Leyson RJF, A personal and provocative view on the European GMO situation. *Eur J Lipid Sci Technol* **105**:471–474 (2003).
- 49 Mitchell P, Europe sees sharp decline in GMO research. *Nature Biotechnol* 21:468–469 (2003).
- 50 Duke SO, Scheffler BE, Boyette CD, Lydon J and Oliva A, Herbicides: biotechnology for control of weeds, in *Encyclopedia of agrochemicals*, vol 2, ed by Plimmer JR, Gammon DW and Ragsdale NN, John Wiley & Sons, New York, pp 733–744 (2003).
- 51 Duke SO, Weeding with transgenes, *Trends Biotech* **21**:192–195 (2003).
- 52 Duke SO, Scheffler BE, Dayan FE and Dyer WE, Genetic engineering crops for improved weed management traits, ACS Symposium Series No 829, American Chemical Society, Washington, DC, pp 52-66 (2002).
- 53 Watrud LS, Lee EH, Fairbrother A, Burdick C, Reichman JR, Bollman M, Storm M, King G and Van de Water PL, Evidence for landscape-level, pollen-mediated gene from genetically modified creeping bentgrass with *CP4 EPSPS* as a marker. *Proc Natl Acad Sci USA* 40:14533-14538 (2004).